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HEADLINE: Latest study of diabetes drug Avandia reaffirms heart risk;
'Black box' warning may not go far enough

BYLINE: Rita Rubin

BODY:

Older patients who took Avandia had a higher risk of heart attacks, congestive heart failure and death than those on other diabetes pills, a study of nearly 160,000 Canadians reports today.

For four years, the study followed patients over age 65, who have the highest rate of type 2 diabetes but aren't well-represented in clinical trials, says lead author Lorraine Lipscombe, a Toronto endocrinologist and researcher at the Institute for Clinical Evaluative Science, funded by the Ontario government.

Lipscombe's team examined how patients fared on Avandia or Actos, the only two drugs in their class, compared with those on other diabetes pills.

Since August, the U.S. labels for Avandia and Actos have carried a "black box" warning against their use in patients with advanced congestive heart failure. However, the new study found Avandia raised heart failure risk even in patients with no history of the condition, suggesting the heart failure warning doesn't go far enough, Lipscombe's team writes in The Journal of the American Medical Association.

About 8% of patients went to a hospital for congestive heart failure or a heart attack during the study. Compared with patients on other diabetes pills, those on only Avandia or Actos had a 60% higher risk of congestive heart failure and a 40% higher risk of heart attack. They also had a 29% higher risk of death.

For reasons not yet clear, the increased heart risks seen in the Avandia/Actos group were predominantly in those on Avandia. That doesn't mean Actos is safer, Lipscombe says. Her study might have had too few Actos patients -- half the number on Avandia -- to detect a higher risk, she says.

In observational studies such as this, factors other than the drugs in question might skew results, so clinical trials that randomly assign patients to treatments are considered the gold standard.

"The problems with the study become obvious with regard to the CHF (congestive heart failure) findings," Nancy Pekarek, spokeswoman for Avandia maker Glaxo-SmithKline, said in an e-mail. "We know (Avandia and Actos) have well-documented and similar CHF events, yet this study somehow finds an increase in these events with Avandia vs. Actos."

But Steven Nissen, the Cleveland Clinic's chief of cardiovascular surgery, says Lipscombe's study "has a lot of appeal. It's independent, it's not funded by industry, and it's huge." And, "it's real-life data."

Nissen reported in The New England Journal of Medicine in May that the pooled results of 42 short-term clinical trials showed Avandia patients were 43% more likely to have a heart attack or be hospitalized for blocked coronary arteries than others in the trials.

Based on Nissen's study and others, the Food and Drug Administration last month added information to Avandia's black box about a potential increased heart attack risk. The FDA has asked Glaxo to compare Avandia's heart attack risk with those of other diabetes pills. That clinical trial is not expected to be done until March 2014.

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